Attachment 1

PERFORMANCE WORK STATEMENT (PWS)
Technical Support Services for Community and Site Specific
Human Health Risk Assessment

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I. PURPOSE

Task orders issued under this Performance Work Statement (PWS) will support EPA's Office of Research and Development (ORD), National Center for Environmental Assessment (NCEA), in developing and updating Provisional Peer-Reviewed Toxicity Value (PPRTV) assessments, as well as research related to prioritizing chemicals for the PPRTV program, expert consultation, and research on cross-cutting issues related to new alternative toxicity data sources and technologies. In addition, this PWS will entail work associated with cumulative risk assessment, including human and non-human biota, and chemical mixtures risk assessment, supporting the advancement of the science in community-based risk assessment.

II. BACKGROUND

Provisional Peer-Reviewed Toxicity Value (PPRTV) Program

NCEA provides health assessments to the Superfund Program through the PPRTV Program. Through PPRTVs, NCEA provides EPA's Office of Solid Waste and Emergency Response (OSWER) with interim toxicity values on accelerated schedules and for chemicals with data that are sufficient to develop screening level values for priority setting but insufficient to support IRIS toxicity values. Chemicals are selected according to priorities set by NCEA and the Superfund Program. PPRTVs are OSWER's preferred source of peer-reviewed health assessments when IRIS values are not available for determining cleanup levels at Superfund sites. Like IRIS assessments, PPRTVs are developed consistent with Agency risk assessment guidelines and methodologies. PPRTVs are available at http://hhpprtv.ornl.gov/.

Integration of New Technologies Into Chemical Safety and Risk Assessment

Evaluation of hazard and dose-response for human health risk assessment (HHRA) of environmental pollutants can be quite challenging in some Agency purviews due to the lack of extant toxicity data. Several initiatives in the public and private sectors over the past decade have resulted in a tremendous increase in the availability of data derived from alternative testing platforms including but not limited to structural read-across/(quantitative) structure-activity relationship ([Q]SAR), in vitro biological activity assays (e.g., ToxCast), toxicogenomics,*in vitro in vivo* extrapolation (IVIVE) reverse toxicokinetic (rTK) modeling, high-throughput (HTP) exposure modeling, and benchmark dose (BMD) modeling. A critical focus area for NCEA is applying emerging science to inform risk screening and assessment.

Cumulative and Chemical Mixtures Risk Assessment

NCEA assists in the development of specific approaches and Agency-wide guidance for cumulative risk assessment and chemical mixtures risk assessment. Developments in this area have received a great deal of interest from US communities, public health advocates and

ecologists. While chemical mixtures risk assessments examine risks to humans and/or biota posed by exposures to multiple chemicals in the environment, cumulative risk assessments entail the analysis of risks posed by exposures to multiple stressors potentially including chemical, physical or biological stressors as well as psychosocial stressors. In addition to analyzing multiple stressors, identifying populations that may be more or less vulnerable than other populations (e.g., the general population) is important for cumulative risk assessments. This could include understanding how certain risk factors affect vulnerability including examination of interactions and delineation of specific mechanisms of the underlying disease etiology. Projects in this area could include the development of specific approaches for assessing cumulative risks to humans and wildlife or risks posed by exposures to chemical mixtures or the conduct of case studies that estimate exposure, dose-response, and human health/ecological risks associated with specific stressors or specific chemical mixtures.

III. SPECIFIC AREAS OF WORK

A. PPRTV Program Support

The purpose of any PPRTV-related task order is to provide services to NCEA, in preparing deliverables to be used by EPA in the future development of the Provisional Toxicity Value (PTV) documents.

The PTV documents are utilized by the Superfund Technical Support Center (STSC) of NCEA in support of the EPA's Superfund Program (SF). The information contained in PTV documents is necessary for developing risk assessments at SF sites (or SF-managed sites) throughout the U.S. The PTV documents provide provisional toxicity values (subchronic and chronic reference doses, subchronic and chronic reference concentrations, oral slope factors, inhalation unit risks, and provisional screening values) if available data are adequate for developing values. Guidance for preparing the toxicity values is identical with Agency methods for developing IRIS values. The PTV documents do not provide toxicity values to replace those currently existing in IRIS.

<u>Specific Requirements</u>

1. The Contractor shall respond to each issued PPRTV related requirement by preparing a Technical Proposal describing how the work will be performed, including deliverables and interim drafts, a schedule, estimated labor hours, cost proposal, and qualifications of personnel by Task. The Contractor shall also prepare a Final Staffing Plan which shows assigned personnel by Task. The Contractor shall provide highly qualified personnel to perform services required under any PPRTV related task orders. At a minimum, major contributors are expected to be Professional Level 4 or 3. The senior contributors shall have earned a terminal degree in their field of expertise (e.g., PhD, ScD, MD, and DVM). Personnel with additional training and certifications (e.g., Diplomate of the American Board of Toxicology (DABT) are highly recommended. Previous experience in developing health assessment documents is required as is a thorough familiarity with EPA guidance utilized for performing health assessments (e.g., 2005 Cancer Guidelines, other IRIS standard operating procedures and guidance, etc.).

2. Through Federal Regulations 48 CFR 46, EPA requires two forms of QA documentation from contractors funded by EPA that conduct environmental data operations on behalf of EPA: (1) documentation of an organization's quality system called a Quality Management Plan (QMP), usually provided at the contract level; and (2) documentation of the application of quality assurance and quality control activities to a project-specific effort, called a Quality Assurance Project Plan (QAPP). The QAPP outlines quality assurance activities to ensure that environmental data are of sufficient quantity and adequate quality for their intended use.

   For each PPRTV-related task order, the Contractor shall prepare and submit a QAPP to address the assigned work. QAPPs are to be compliant with EPA/R-5, EPA's requirements for Quality Assurance Project Plans for organizations that conduct environmental data operations, available at https://www.epa.gov/sites/production/files/2015-07/documents/r5-final.pdf . Guidance and specifications for preparing QAPPs for activities funded by the EPA are outlined in EPA QA/G-5, available at https://www.epa.gov/quality/guidance-quality-assurance-project-plans-epa-qag-5. Quality specifications for non-EPA organizations are available at https://www.epa.gov/quality/quality-specifications-non-epa-organizations-do-business-epa.

3. The Contractor will conduct a comprehensive literature search and prepare Scoping Documents (table and associated text) for each of the chemicals to be evaluated under any PPRTV task order. The Contractor shall use EPA's Health and Environmental Research Online (HERO) database and other appropriate databases for literature search and retrieval. The Contractor shall be required to follow EPA policies regarding the use of EPA websites and software, as well as applicable copyright and security laws. The scoping table should include, at minimum, the number of studies, title of study, author(s), and study type. In addition to the Scoping Documents, the Contractor will compile and submit an EndNote® library for each chemical, as well as the Boolean search strings and any other relevant search strategy information applied for each chemical. Prior to developing the libraries for these chemicals, the Contractor will brief EPA about the EndNote® library structure envisioned for this task order. This briefing will ensure the format is appropriate for reviewing the literature search results.

4. The Contractor shall prepare the PTV documents for specific individual chemicals as directed by EPA.

5. After review of any deliverables or during the EPA's subsequent processing, EPA may require revisions to the PTV deliverables. When necessary, EPA will provide detailed requirements for revisions to the Contractor. The Contractor shall submit a plan to respond to the comments and communicate that plan to EPA. After obtaining EPA agreement with the plan, the Contractor shall proceed with the revision work and deliver revised deliverables that address each element of EPA comments. Additional revisions may be necessary on rare occasions.

Required work will be described in specific Task Order PWSs. Each Task Order PWS will be submitted by the EPA Task Order Contract Officer Representative (TOCOR) to the EPA Contracting Officer (CO) for delivery to the Contractor via a Request for Proposal (RFP). Upon receipt of the RFP from the CO, the Contractor prepares and submits a proposal describing how the work will be performed. For each Task Order, the Contractor also prepares and submits a Quality Assurance Project Plan (QAPP) to address the assigned work. Individual Task Order PWSs will include additional details, as applicable. After any necessary clarifications are received, the proposal is approved by the CO through issuance of a task order document. Upon receipt of a task order document, work may commence in accordance with tasking and schedules specified in the issued task order. Each TOCOR will have the authority to issue technical direction.

The Contractor shall provide all technical support within the scope of this PWS. The Contractor shall perform tasks, as specified by individual task orders issued by the CO. Task orders, commonly require expertise in multiple disciplines such as epidemiology, toxicology, ecotoxicology, pharmacology, physiology, pathology, chemistry, public health, quantitative dose-response modeling, biostatistics, and mathematical modeling, including benchmark dose (BMD) modeling, physiologically-based pharmacokinetic (PBPK) modeling, exposure modeling, library science, and technical editing. For many tasks, scientific needs are highly specialized, requiring expert personnel having the knowledge and ability to fully and critically evaluate study methodologies and results in the technical disciplines identified above. Analyses must be scientifically sound and sufficiently documented to withstand intensive critical examination and review by other experts in the relevant disciplines.

For performance of work under this PWS (including for performing literature searches, citing references, and generating bibliographies), the Contractor will be required to use the HERO database, a database of scientific studies and other references used to develop EPA's risk assessments. HERO is developed and managed in ORD by NCEA. EPA shall provide the Contractor with the necessary training and access to the database. Access to HERO is granted to an individual on a limited access basis and for a specific period of time in order for approved work to be completed.

B. Integration of New Technologies Into Chemical Safety and Risk Assessment

Several EPA programs and regions are often tasked with addressing the potential hazard(s) to human health and the environment of chemicals for which little-to-no data exist. Examples include, but are not limited to, OSWER/Office of Superfund Remediation and Technology Innovation (OSRTI's) assessment of Superfund sites, OW's Unregulated Contaminant Monitoring Rule (UCMR) efforts, and the screening of thousands of compounds under Office of Chemical Safety and Pollution Prevention (OCSPP's) purview. The shared need in this risk decision context warrants basic identification of hazard and associated dose-response for screening and prioritization purposes. Considering the lack of repeat-dose study data for a significant number of potentially hazardous chemicals of interest to EPA offices, alternative toxicity methods and data may fill a critical need. The acquisition of alternative data outputs will be tasked to EPA's National Center for Computational Toxicology (NCCT) in collaboration with NCEA. The alternative data task(s) encompassed in this PWS will involve/support methods

development and proof-of-concept evaluations that inform how data from the aforementioned alternative platforms may ultimately result in the identification of hazard and associated quantitative screening estimates, and other fit-for-purpose applications for large numbers of chemicals, as well as the application of such screening estimates into HHRA technical support products delivered to end-users by NCEA.

C. Cumulative and\or Chemical Mixtures Risk Assessment

The contractor shall support the advancement of cumulative risk assessments (CRAs) and related research at the EPA through development of CRA methods or relevant case studies. Methods development has been highlighted as a current need to further integrate exposures to non-chemical stressors and incorporate ecological receptors into CRAs. There have also been calls for methods to aid in the identification of vulnerable populations. Support may entail the development or application of specific methods within a CRA (e.g., dose-response assessment of non-chemical stressors, integration of ecological and human health endpoints or developing joint distributions of exposures to multiple stressors) or the development of a case study that includes any of the following steps: problem formulation, hazard identification, dose-response assessment, exposure assessment, and risk characterization. The stressors included in such methods development or case studies might include multiple chemicals (i.e., mixtures) or combinations of multiple chemical and non-chemical (e.g., physical, biological or psychosocial stressor) exposures. Support may also entail the examination of the influence of different stressors (e.g., including but not limited to the following: pre-existing diseases such as diabetes, genotypic differences, or socioeconomic factors) on exposure- or dose-response relationships, including interactions between chemical and non-chemical stressors. Specific contract support activities might include (but not be limited to): (1) Methods development or case studies to evaluate combinations of multiple chemical and non-chemical (e.g., physical, biological or psychosocial stressor) exposures in humans and biota; (2) Characterization of interactions between chemical and non-chemical stressors or among non-chemical stressors in a CRA context/framework; and (3) Characterization of the influence of population-level vulnerabilities on exposure- or dose-response to a group of stressors.

D. Identifying and Selecting Pertinent Studies: Literature Search and Screening for Alternative Data, Cumulative, and/or Mixtures Assessment products

The contractor shall conduct and document literature searches. The goal of the search strategy is the same whether it be for alternative data application research or for cumulative mixtures assessment. That is to identify full reports of primary studies (i.e., original sources of data) pertaining to key question(s) pertinent to the research focus of a given task order. These studies can be published papers or unpublished reports, but need to provide sufficient detail to allow evaluation of the study methods. The initial search strategy “casts a wide net”; subsequent steps in the process are used to screen and exclude articles that are not relevant, and to sort the relevant studies into categories (e.g., experimental studies in animals, observational studies in humans) for further evaluation.

Literature search support may include conducting comprehensive literature searches to identify all literature relevant to the health effects of a particular chemical, literature search updates, or focused literature searches.

Unless otherwise specified, searching and related activities shall be performed using EPA's HERO interface, and literature search products shall be uploaded to a HERO project page. The Contractor shall work with EPA's HERO librarians as necessary in providing IRIS literature search support.

In general, searches shall include on-line databases (e.g., PubMed), relevant domestic and international non-periodical literature (e.g., technical reports, monographs, and conference proceedings), other secondary sources (e.g., National Toxicology Program, Toxic Substance Control Act (TSCA) Test Submissions [TSCATS] Database, and Agency for Toxic Substances Disease Registry [ATSDR] Toxicological Profiles), appropriate EPA health assessment documents, federal docket submission.

In conducting a comprehensive literature search, the Contractor shall identify all studies of relevance to the product or assessment, including all health effects in animals and humans resulting from inhalation, oral, dermal, intraperitoneal, and intravenous exposure studies. The Contractor shall also identify data specifically useful to addressing risks to children and other susceptible populations. The Contractor will also include other relevant studies such as in vitro studies related to mechanism of action; studies of absorption, distribution, metabolism, and elimination; models useful for dose response assessment such as dosimetry models and physiologically-based pharmacokinetic (PBPK) models; and studies useful for elucidating modes of action (MOA). Additionally, the Contractor shall identify other resource information such as reviews, editorials, exposure studies, and methods studies.

Screening for determination of relevance and type of reference (e.g., human epidemiology study, animal bioassay, or review paper) shall initially be based on review of the title and abstract, and in rare cases, the full text of the article. References shall be assigned HERO "tags" during this screening.

The Contractor shall provide a list of documents available in foreign language only (e.g., using a tag in HERO). EPA will identify those foreign language papers of interest. The Contractor will proceed with translation of papers only after providing the EPA with a price quote for translation and EPA approval. The initial cost estimate should not include estimated costs associated with translation.

Specific direction related to literature search and screening will be provided in individual task orders and technical direction.

E. Quantitative Dose-Response Analysis for Alternative Data, Cumulative, and/or Mixtures Assessment products

The contractor shall support the development of quantitative dose-response analyses, including text and modeling results. This may include: (1) benchmark dose modeling for the

determination of point of departure for effects; (2) development and/or application of dosimetry models, physiologically-based pharmacokinetic (PBPK) models, or other types of biologically-based dose response (BBDR) models; (3) other specialized quantitative analysis, including time-to-tumor modeling and life table analysis; and (4) where appropriate, derivation of reference doses (RfDs), reference concentrations (RfCs), slope factors and inhalation unit risks. The Contractor shall also use NCEA guidelines, handbooks and other resource materials for more information regarding dose-response analysis. The Contractor may be asked to use certain tools (e.g., WIZARD) for performing these analyses (required database to be provided by EPA).

All work shall be conducted and reported consistent with EPA's *Benchmark Dose Technical Guidance Document* (BMDS), the most recent version of BMDS, other relevant EPA guidelines (e.g., 1994 *Methods for Derivation of Inhalation Reference Concentrations (RfCs) and Application of Inhalation Dosimetry*), NCEA's *Annotated Checklist of Best Practices for Dose-Response Analyses for IRIS* (to be provided to the Contractor), and/or literature pertinent to methodologies that may be required for completion of BMD related tasks (e.g., Thomas et al., 2011). The Contractor shall perform QA checks on all data input and results of quantitative modeling, develop and maintain internal documentation and data, and deliver to EPA all input data, files, code, and documentation (in electronic format) in order that results can be replicated.

Specific direction related to quantitative dose-response analysis will be provided in individual task orders and through technical direction. This could include unique direction for developing dose-response assessments for non-chemical stressors either individually or in combination with other chemical or non-chemical stressors. It could also include the development of dose-response functions in vulnerable populations.

F. General Support in Development of PPRTV Assessments, Alternative Data, Cumulative, and/or Mixtures Assessment products

Although not all metrics below will be pertinent across the support foci presented in this PWS, general support in one or more areas may be needed for tasks related to product/assessment development, including, but not limited to:

- Development of brief descriptions of the substance's physical-chemical properties
- Summaries of exposure information and characterization of exposure potential
- Summaries of hazard identification and/or dose-response conclusions from other governmental or international health assessment bodies
- Integrated synthesis of information on absorption, distribution, metabolism, and elimination (ADME) for individual chemicals
- Summary tables for individual, subchronic and chronic human studies, animal bioassays, and/or ecological/ecotoxicology studies, that include information on study design and results
- Discussions of susceptible subpopulations, such as children

Specific direction related to general support tasks relevant to a given thematic focus area will be provided in individual task orders and through technical direction.

IV. Analysis, Document and Issue Paper Preparation

The contractor shall provide production support for drafting of scientific and technical products that are produced during the development of alternative data case study examples and any associated conceptual document(s) and/or products or documents associated with cumulative mixtures assessment task(s). The contractor shall develop analyses, white papers, scientific publications, or reviews of specific health/exposure assessment topics pertinent to the foci proposed in this PWS. The proposed scientific and technical authors shall be recognized nationally or internationally in their fields, and they shall have the general knowledge, expertise, or experience, specified in the task order. The selected author/consultant must have experience that includes authoring several journal articles or other technical documents that specifically relate to the topic. During the development of the documents or issue papers, the Contractor may be required to meet with the EPA and/or the authors to discuss the documents or issue papers. Subjects of documents or issue papers vary widely and will be defined specifically by the COR. Specific direction related to production support will be provided in individual task orders and through technical direction.

V. PRODUCT QUALITY

A. General Health Assessment Provisions

In the preparation of any of the scientific documents required by a task order, the Contractor may be required to provide the services of experts in the areas of epidemiology, toxicology, ecotoxicology, pharmacology, physiology, pathology, chemistry, public health, quantitative dose-response modeling, biostatistics, mathematical and biological modeling, exposure modeling, library science, and technical editing. In many of the tasks, the scientific needs are highly specialized; this requires expert personnel with the knowledge and ability to fully and critically evaluate study methodologies and results in the technical disciplines identified above. Unless otherwise specified in a task order, products prepared must be state-of-the-art analyses based on expert critical evaluation and analysis of the health effects data. Work products are expected to provide scientifically and defensible evaluations that accurately reflect current scientific knowledge, risk assessment methods, and EPA guidelines and approaches.

B. Quality Assurance/Quality Control Requirements

The contractor's QMP must be approved by the NCEA Director of Quality Assurance (DQA) or Quality Assurance Manager (QAM) prior to any work under the contract. Documents specifying the requirements and guidance for developing the QMP can be found at EPA's website for QMPs (http://www.epa.gov/quality/epa-qar-2-epa-requirements-quality-management-plans).

All work to be conducted by the contractor shall be directed by individual Task Orders. If specified within a Task Order, the contractor shall develop a Quality Assurance Project Plan (QAPP) in accordance with *U.S. EPA requirements for Quality Assurance Project Plans* (EPA QA/R-5) at https://www.epa.gov/sites/production/files/2015-07/documents/r5-final.pdf, and provide a QAPP to the TOCOR and the NCEA QA Manager in electronic form for approval. The QAPPs should demonstrate a clear understanding of each task order's project

goals/objectives/questions and issues, address data collection, analysis, and the use of existing data. QAPPs shall indicate how type, quantity, and quality of data will be quality assured and maintained. The EPA QA Manager reviews the status of projects with regards to QAPP approvals, QA reports and QC documentation, and correction of any findings from audits, if a QA audit is conducted. The contractor shall comply with the QAPPs. Guidance for developing EPA-compliant QAPPs can be found at https://www.epa.gov/sites/production/files/2015-06/documents/g5-final.pdf

C. Written and Electronic Products

The Contractor shall provide written and electronic products of high quality, written in a clear, concise style, with a logical organization and presentation. The Contractor shall:

- Prepare documents consistent with EPA templates, handbooks, and guidance as specified in the task order.
- Perform scientific and technical editing of all products.
- Provide documents that accurately and completely summarize the information subject to review, extraction, and/or analysis.
- Present scientific information in a consistent style that makes it easy for the reader to follow and pay specific attention to ensure consistent and accurate information content, and appropriate data interpretation.
- Provide all appropriate documentation sufficient to allow all analyses to be replicated.

Products not adhering to these standards and guidelines or substantially lacking scientific quality will not be accepted.

VI. OTHER REQUIREMENTS

1. For each task order, the Contractor shall certify that, to the best of the Contractor's knowledge and belief, there are no relevant facts or circumstances which could give rise to an organizational conflict of interest, as defined in FAR 9.5, or that the Contractor has disclosed all such relevant information. The Contractor shall provide the following conflict of interest certification within fifteen (15) calendar days after issuance of each task order:

   > I certify that, to the best of my knowledge and belief, no actual, apparent, or potential organizational or individual conflicts of interest related to this task order exist. Personnel who perform work under this task order, or relating to the task order, have been informed of their obligation to report personal and organizational conflicts of interest. All actual, apparent or potential organizational or individual conflicts of interest related to this task order have been reported to the Contracting Officer and Task Order Contracting Officer Representative (TOCOR) or are attached, if applicable.

2. Prior to commencement of any work, the Contractor agrees to notify the CO and TOCOR, that to the best of its knowledge and belief, no actual or potential conflict of

interest exists or to identify to the CO and TOCOR any actual or potential conflict of interest the Contractor may have. In urgent situations, however, work may begin but notification shall be made within five (5) working days.

3. If an actual or potential organizational conflict of interest is identified during the performance, the Contractor shall immediately make a full disclosure in writing to the CO and TOCOR. This disclosure shall include a description of actions that the Contractor has taken or proposes to take, after consulting with the CO, to avoid, mitigate, or neutralize the actual or potential conflict of interest. The Contractor shall continue performance until notified by the CO of any contrary action to be taken.

4. The Contractor shall be responsible for obtaining a conflict of interest certification for any subcontractor or consultant services.

5. All specific task orders under this agreement shall be cost tracked by chemical or individual tasks.

6. All deliverables will be reviewed for conformance to the requirements of this PWS before being approved as final.

7. In the course of conducting this work, the Contractor will interface with scientists in ORD, NCEA and potentially other laboratories, Centers and Offices. The Contractor shall clearly identify itself as a Contractor when in attendance at EPA meetings and other functions relevant to this procurement. The Contractor's representative or other Contractor personnel shall identify themselves as contract personnel when placing calls to the CO and TOCOR in conjunction with activities described in the PWS. The Contractor will be responsible for keeping minutes of the meetings, whether in person or by telephone conference, and shall provide the minutes to the TOCOR for review and acceptance.

8. Any publications resulting from this procurement will be subject to NCEA and ORD peer review and clearance procedures as required.

9. EPA shall be mentioned as the funding source, with appropriate and standard EPA disclaimers, for subsequent articles and publications that arise as a result of the research provided for this project, its results and products, and subsequent work stemming from products after the project is formally closed.

10. Progress reports shall be provided monthly, along with invoices indexed to billing DCN numbers, summarizing the work status and costs associated with all tasks being performed under this Agreement.

VII. NOTICE REGARDING SERVICES PROVIDED UNDER THIS PWS

The Contractor is strictly limited to providing technical and analytical services. The Contractor

shall not engage in activities of an inherently governmental nature such as the following:

(1) Formulation of Agency policy
(2) Selection of Agency priorities
(3) Development of Agency regulations

Should the Contractor receive any instruction from an EPA staff person that the Contractor ascertains to fall into any of these categories or goes beyond the scope of the PWS or any task order PWS, the Contractor shall immediately contact the CO and TOCOR.